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Induction of DEL Recombination in the Yeast *Saccharomyces cerevisiae* Using a Microtiter Plate Assay Format

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ABSTRACT

It has been established that a number of mammalian tumors are associated with genomic rearrangements. A system designed to detect genomic rearrangements has been constructed in the yeast *Saccharomyces cerevisiae*. This system consists of a heterozygous duplication of the *his3* gene in which one copy has been deleted at the 3′ end and the other deleted at the 5′ end (Schiestl et al., 1988). Both copies of the *his3* gene are nonfunctional. This duplication of the *his3* gene is separated by the *LEU2* gene and pBR322 plasmid sequences. Homologous intrachromosomal recombination between the *his3* duplications regenerates an intact *HIS3*$^+$ allele, while deleting the intervening *LEU2* gene and pBR322 DNA. The assay has been accordingly named the yeast DEL (deletion) assay. It has been shown previously that this recombination event is inducible by a variety of chemicals, as well as ultraviolet light and ionizing radiation (Schiestl, 1989; Schiestl et al., 1989). In this work we report the conversion of the yeast DEL assay to a microtiter plate format, which greatly increases its ease of use and quantitative accuracy. Using the microtiter plate format we have found yeast DEL recombination to be inducible by the carcinogens 4-nitroquinoline oxide, epichlorohydrin, methyl methanesulfonate, ethyl methanesulfonate, benzene, and formaldehyde. Chemicals that do not induce DEL recombination include dimethylsulfoxide, acetone, ethanol, L-methionine, and methyl orange. In this format the Yeast DEL Assay is easier to use than the traditional agar plate assay. Results are obtained in 2–3 days, and the labor required is approximately half that required to perform the assay using the agar plate method. The new format, in which microtiter plate wells containing recombinant yeast colonies are scored by color change of the pH indicator dye, methyl orange, is especially amenable to automation.

INTRODUCTION

The association of genome rearrangements and deletions with mammalian cancers, including retinoblastoma, lung cancer, melanoma, neuroblastoma, breast cancer, kidney cancer, colorectal cancer, and leukemia, has been well established (see Cairns, 1981; Hansen and Cavenee, 1988; Klein, 1981; Stanbridge, 1990; Muller and Scott, 1992; Miyao et al., 1993; Reiter et al., 1993; Marchetti et al., 1993; Zalupski et al., 1990; Yang-Feng et al., 1993; Dyer et al.,

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